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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,000	05/16/2005	Masakazu Hatano	05318/HG	1933

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EXAMINER	
HUANG, GIGI GEORGIANA	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,000	HATANO ET AL.	
	Examiner	Art Unit	
	GIGI HUANG	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *5-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/16/2005, 6/27/2005, 8/16/2007, 4/21/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I in the reply filed on September 30, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

2. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. The claim is not yet perfected.

Status of Application

3. Applicant has elected Group I in response to restriction requirement for the examination.

Due to restriction, based on election of Group I, claims 5-12 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Claims 1-4 are present for examination at this time.

Information Disclosure Statement

5. The information disclosure statement filed 5/16/2005, 6/27/2005, 8/16/2007 fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because there is no translation provided for several references which are designated in the respective IDS.

It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Instant claims 1-4 are directed to a compound defined by reference to desirable characteristics or properties, namely, that the active ingredient is a "rho kinase inhibitor".

The term "Rho kinase inhibitor" is not defined and it does not address which combination of receptors are target, the amount of binding desired for the receptors, and the compounds that would accomplish this other than (R)-trans-N- (pyridin- 4-yl)-4-(1-aminoethyl)cyclohexane carboxamide, (R)- (+)-N- (1H-pyrrolo [2,3-b] pyridin- 4-yl)-4-

(1-aminoethyl)benzamide, 1-(5- isoquinoline sulfonyl)-homopiperazine, or 1-(5-isoquinoline sulfonyl)- 2 –methylpiperazine which is disclosed in the specification.

The term "Rho kinase inhibitor " is not adequately described as it is defined by a functional characteristic where it is defined by what it *does* and not what it *is*. Second, it does not describe adequately the degree of access, binding, or activity to the receptor to ascertain what compounds would fulfill the description. As a result, the fact pattern indicates that the artisan was not in possession of the claimed method of use.

The claims cover all compounds having these characteristics or properties, whereas the application provides support for only some compounds within the scope of what is claimed. However, there is no evidence that there is any per se structure/function relationship between the disclosed four compounds and any others that might yet to be found. There are no structural identifying characteristics or common structural cores presented for the claimed group of compounds. Therefore, the claimed invention is not supported by adequate written description.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation or any combination thereof. In the instant, the only factor present in the claims is a recitation of board classes of active agents, which encompass compounds with varying structure, activities and pharmacological profiles. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the

specification does not provide adequate written description of the claimed genus, aside from the specific compounds recited in the specification. The recited genus of active agents is so broad that the claims effectively read on any and all biological chemical compounds.

Thereby, while having written description for (R)-trans-N- (pyridin- 4-yl)-4- (1-aminoethyl)cyclohexane carboxamide, (R)- (+)-N- (1H-pyrrolo [2,3-b] pyridin- 4-yl)-4- (1-aminoethyl)benzamide, 1-(5- isoquinoline sulfonyl)-homopiperazine, or 1-(5-isoquinoline sulfonyl)- 2 -methylpiperazine, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims, and only those compounds are to be considered.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1-3 are rejected under 35 U.S.C. 102(e) as being anticipated by Dole et al. (U.S. Pat. Pub. 20050014783).

Dole et al. teaches the therapeutic combination of rho-kinase inhibitors such as fasudil (1-(5- isoquinoline sulfonyl)-homopiperazine or HA-1077 or AT-877) and Y-27632 ((R)-trans-N- (pyridin- 4-yl)-4- (1-aminoethyl)cyclohexane carboxamide) with

other agents including beta blockers for cardiovascular ailments (Abstract, Paragraph 6-22, 29). The compositions can be in several forms including tablets, capsules, solutions (paragraph 94, claims 1-7, 9).

All the critical elements are taught by the cited reference and thus the claims are anticipated.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dole et al. (U.S. Pat. Pub. 20050014783) as applied to claim 1-3 above, and in view of Jin et al. (U.S. Pat. 6187304).

The teachings of Dole et al. are addressed above.

Dole et al. does not expressly teach the use of timolol, befunolol, carteolol, nipradilol, betaxolol, levobunolol, or metipranolol.

Jin teaches that ß-adrenergic receptor blocking drugs (beta-blockers) such as timolol, carteolol, or betaxolol have been used extensively for hypertrophic cardiomyopathy and its benefits (Col. 4 lines 6-14).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use known beta blockers such as timolol, as suggested by Jin et al., and produce the instant invention. It would have been obvious to one of

skill in the art to use known beta-blockers such as timolol, carteolol, or betaxolol known the art to be useful for cardiomyopathy in the combination taught by Dole.

One of ordinary skill in the art would have been motivated to do this because it is desirable to use known products useful and beneficial for the combination treatment taught by Dole.

12. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Azuma et al. (WO 00/09162).

It is noted that U.S. Pat. 6673812 will be used as the translation of the WIPO document. All references will be to the U.S. Pat.

Azuma et al. teaches a composition for glaucoma comprising a rho kinase inhibitor(Abstract). Azuma teaches the compositions can be in several forms including tablets, capsules, liquids, and drops. Azuma exemplifies the compositions including an eye drop comprising (R)- (+)-N- (1H-pyrrolo [2,3-b] pyridin- 4-yl)-4- (1-aminoethyl)benzamide (also known as Y-39983, Col. 22-Example 7, Claim 1, 8-9) and that the compound (labeled Compound D) had a long lasting affect (Col. 25.line 12-13). Azuma also teaches that beta blocker such as timolol are widely used for glaucoma as they lower intraocular pressure (Col. 1 line 39-43).

Azuma et al. do not expressly teach a composition with the combination of a rho-kinase inhibitor and a beta-blocker.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine two drugs known to be effective for the same purpose as addressed by Azuma, and produce the instant invention.

As addressed in Azuma, beta-blockers are widely used for the treatment of glaucoma, and rho kinase inhibitors (exemplified by (R)- (+)-N- (1H-pyrrolo [2,3-b] pyridin- 4-yl)-4- (1-aminoethyl)benzamide) are also taught be useful for glaucoma, it is obvious to combine two drugs useful for same purpose in order to form third composition that is to be used for very same purpose; the idea of combining them flows logically from their having been individually taught in prior art.

One of ordinary skill in the art would have been motivated to do this because it is desirable to have and produce a composition comprising many components which have desirable effects for the condition resulting in the additive effect of the ingredients for glaucoma. One would have been motivated to do this because it is desirable to produce a combination drug to be effective for as may conditions as possible as it would not only increase the drugs' versatility by being effective for the condition to be addressed, but also increase sales with nominal development.

13. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeSantis (U.S. Pat. 5502052) in view of Kapin (WO97/23222).

DeSantis teaches compositions for combination therapy comprising beta-blockers for glaucoma. The beta-blockers taught include timolol, befunolol, carteolol, nipradilol, betaxolol, levobunolol, and metipranolol. DeSantis also teaches that for a significant number of glaucoma patients, more than one drug is need to achieve

therapeutic control of the glaucoma and as a result two or more different types of drugs are sometime required to achieve therapeutic control. The compositions can be in various form including solution, gel, emulsions. An example with betaxolol is taught with a para-amino clonidine (see full document, specifically Abstract, col. 1 line42-50, Col. 2 line15-23, 34-48, Col. 3 line 1-7, col. 5 line 20-35, 41-43, col. 6 line 7-40).

DeSantis does not expressly teach a composition with the combination of a rho-kinase inhibitor and a beta-blocker.

Kapin et al. teaches compositions comprising certain isquinolinesulfonyl compounds for the treatment of glaucoma. The preferred compound is fasudil. (see full document, specifically Abstract, Page 5-6, 8-11, Claim 1-3).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to include fasudil, as suggested by Kapin, and produce the instant invention.

As addressed in DeSantis, beta-blockers are widely used for the treatment of glaucoma, and therapeutic control of the glaucoma frequently cannot be achieved by one drug alone and combinations are use to attain the therapeutic control. Kapin taught fasudil be useful for glaucoma, it is obvious to combine the drugs which are useful for same purpose in order to form third composition that is to be used for very same purpose; the idea of combining them flows logically from their having been individually taught in prior art as DeSantis teaches that combination therapy is known in the art.

One of ordinary skill in the art would have been motivated to do this because it is desirable to have and produce a composition comprising many components which have

desirable effects for the condition resulting in the additive effect of the ingredients for glaucoma. One would have been motivated to do this because it is desirable to produce a combination drug to be effective for as may conditions as possible as it would not only increase the drugs' versatility by being effective for the condition to be addressed, but also increase sales with nominal development.

Conclusion

14. Claims 1-4 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GIGI HUANG whose telephone number is (571)272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fredrick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GH
/Zohreh A Fay/
Primary Examiner, Art Unit 1612